

**Remarks**

Claims 1-3, 12-13, 21-23, 37-38, 41-45, 48-52, 58, 61, and 64 are pending. Claims 37-38, 41-45, 48-52, 58, 61, and 64 are withdrawn. Claims 1, 12-13, and 21-23 have been amended. Claims 1, 12-13, and 21-23 were amended to more clearly claim what applicants consider to be their invention. Claims 142-146 are newly added. Support for newly added claims 142-144 can be found in claim 12, and throughout the specification. Support for newly added claims 145 and 146 can be found in the specification on page 29, lines 11-15, for example.

Claims 1 and 13 have been amended to recite that the epithelial cells are contacted with an effective amount of  $Zn^{2+}$  and one or more of the following molecules: ATP; ivermectin;  $\alpha$ ,  $\beta$ -methylene-ATP; benzoyl-benzoyl-ATP; ATP $\gamma$ S; or AMPPNP. Therefore, the claim was changed to reflect that *both*  $Zn^{2+}$  and one or more of the other molecules are included. Claim 22 was similarly amended to recite that the contacting step is performed with a  $Zn^{2+}$  and ATP; ivermectin;  $\alpha$ ,  $\beta$ -methylene-ATP; benzoyl-benzoyl-ATP; ATP $\gamma$ S; or AMPPNP-containing inhalant, nebulization, aerosol, or instillant. Support for these amendments can be found, for example, on page 28, lines 5-8 of the specification.

Claims 1 and 13 were amended to recite that there is a sustained elevation in cytosolic  $Ca^{2+}$  levels in the cell. Support for this amendment can be found, for example, on page 4, lines 10-12 and on page 38, lines 7-12.

Claims 12 and 21 were amended to remove the words “the cell’s” in order to clarify the nature of the invention. Support for this amendment can be found in the original claims, throughout the application, and specifically on page 8, lines 5-21, and page 16, lines 17-18

Claim 23 was recited to change the word “zinc” to “ $Zn^{2+}$ ” to properly depend from claim 13.

**Claim Rejections – 35 USC § 102**

Claims 1-2, 12-13, and 21-22 have been rejected under 35 U.S.C. 102(b) for allegedly being anticipated by U.S. Patent 5,840,278 (Coleman et al.). Specifically, the Office Action

ATTORNEY DOCKET NO. 21085.0044U3  
Application No. 10/542,555

states that Coleman et al. teaches administering via aqueous nasal spray a composition that contains, *inter alia*, 35 mg zinc, 106 mg calcium, and sodium bicarbonate in 1.5 fluid ounces.

For a prior art reference to anticipate a claimed invention, each and every element of the claimed invention must be disclosed in that single reference. Further, the disclosure in that single reference must be enabling. If one element of the claimed invention is not disclosed in the prior art reference, there is no anticipation. It is settled law that “[a] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently.”

*Verdegaal v. Union Oil*, 814 F2d. 628, 2 USPQ2d 1051 (Fed. Cir. 1987).

Claims 1 and 13 have been amended herein by adding the limitation that the epithelial cells are contacted with  $Zn^{2+}$  and one or more of the following molecules: ATP; ivermectin;  $\alpha$ ,  $\beta$ -methylene-ATP; benzoyl-benzoyl-ATP; ATP $\gamma$ S; or AMPPNP.

Coleman et al. does not teach using both zinc and ATP; ivermectin;  $\alpha$ ,  $\beta$ -methylene-ATP; benzoyl-benzoyl-ATP; ATP $\gamma$ S; or AMPPNP. Because Coleman et al. does not teach each and every element of amended claims 1 and 13 and those claims that depend there from, there is no anticipation. Therefore, applicants believe these amendments overcome the rejections and respectfully request withdrawal of these rejections and allowance of amended claims 1 and 13, and dependent claims 2, 13, and 21-22.

Therefore, applicants respectfully request withdrawal of this rejection.

Claims 1-2, 12-13, and 21-23 have been rejected under 35 U.S.C. 102(b) for allegedly being anticipated by U.S. Patent 5,622,724 (Bryce-Smith et al.). Specifically, the Office Action states that Bryce-Smith et al. discloses treating symptoms of the common cold by administering a spray of a solution containing symptom effective treating amount of a solution of substantially unchelated ionic zinc compound to the nostrils and respiratory tract of a patient in need thereof.

As discussed above, for a prior art reference to anticipate a claimed invention, each and every element of the claimed invention must be disclosed in that single reference. Further, the disclosure in that single reference must be enabling. If one element of the claimed invention is not disclosed in the prior art reference, there is no anticipation. It is settled law that “[a] claim is

anticipated only if each and every element as set forth in the claim is found, either expressly or inherently.” *Verdegaal v. Union Oil*, 814 F2d. 628, 2 USPQ2d 1051 (Fed. Cir. 1987).

Claims 1 and 13 have been amended herein by adding the limitation that the epithelial cells are contacted with  $Zn^{2+}$  and one or more of the following molecules: ATP; ivermectin;  $\alpha$ ,  $\beta$ -methylene-ATP; benzoyl-benzoyl-ATP; ATP $\gamma$ S; or AMPPNP.

Bryce-Smith et al. does not teach using both zinc and ATP; ivermectin;  $\alpha$ ,  $\beta$ -methylene-ATP; benzoyl-benzoyl-ATP; ATP $\gamma$ S; or AMPPNP. Because Bryce-Smith et al. does not teach each and every element of amended claims 1 and 13 and those claims that depend there from, there is no anticipation. Therefore, applicants believe these amendments overcome the rejections and respectfully request withdrawal of these rejections and allowance of amended claims 1 and 13, and dependent claims 2, 12, and 21-23.

Therefore, applicants respectfully request withdrawal of this rejection.

### **Claim Rejections – 35 USC § 103**

Claims 1-3, 12-13, and 21-23 are rejected under 35 U.S.C. 103(a) for allegedly being unpatentable over the combined teachings of Taylor et al. and Schwiebert et al. in view of CAPLUS abstract 2001:30580 (herein referred to as Sperlagh et al.). Specifically, the Office Action states that Taylor et al. discloses that P2X purinergic receptor channels bind ATP and mediate  $Ca^{2+}$  influx and signals that stimulate secretory  $Cl^-$  transport across epithelia. The Office Action goes on to state that the P2X receptors can be targeted to treat cystic fibrosis.

The Office Action states that Schwiebert et al. discloses that P2X receptors, on binding their ATP target, may increase cytosolic  $Ca^{2+}$  transiently and stimulate  $Cl^-$  and fluid secretion and ciliary beat frequency. The Office Action goes on to state that purinergic agonists have been used to stimulate  $Cl^-$  and fluid secretions from cystic fibrosis tissues and epithelial cell models from the lung and airways and from the GI systems. The Office Action states that in cystic fibrosis,  $Cl^-$  and fluid secretion are lacking but sodium absorption is augmented.

The Office Action states that Sperlagh et al. is cited to establish that zinc ion is a known P2X receptor modulator that potentiates the actions of ATP and P2X receptor gated ion channels.

The Office Action alleges that the ordinary skilled artisan would have been motivated to utilize the known agonist, zinc ion, to treat cystic fibrosis. The Office Action also alleges that combined therapy with ATP is suggested from their coaction on the ion channels to bring about Cl<sup>-</sup> transport and increased Ca<sup>2+</sup>. The Office Action also alleges that zinc chloride is suggested from its common availability as a zinc ion source. The Office Action also alleges that high calcium concentration is suggested from the known effect of calcium to activate epithelial chloride channels. The Office Action alleges that in cystic fibrosis, sodium absorption is augmented, so lower sodium concentration in the treatment medium is suggested. The Office Action further alleges that lower magnesium in the treatment is suggested in order to control one more variable in the complicated cascade of factors. The Office Action alleges that the ordinary skilled artisan would have been motivated to deliver the treatment composition via conventional means to access the target cystic fibrosis diseased cells, e.g., via nasal spray, nebulizer, or aerosol inhaler.

The U.S. Patent and Trademark Office has the burden under 35 U.S.C. § 103 to establish a *prima facie* case of obviousness. See *In re Warner et al.*, 379 F.2d 1011, 154 U.S.P.Q. 173, 177 (C.C.P.A. 1967); *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598-99 (Fed. Cir. 1988). “It can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references.” *Id.* Moreover, in rejecting a claim under 35 U.S.C. § 103, the Examiner must establish a *prima facie* case that: (i) the prior art suggests the claimed invention; and (ii) the prior art indicates that the invention would have a reasonable likelihood of success. See *In re Dow Chemical Company*, 837 F.2d 469, 5 U.S.P.Q.2d 1529 (Fed. Cir. 1988). In order for a reference to be effective prior art under 35 U.S.C. § 103, it must provide a motivation whereby one of ordinary skill in the art would be led to do that which the appellant has done. See *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1535, 218 USPQ 871, 876 (Fed. Cir. 1983). “One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention.” *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988). “When the references cited by the examiner fail to establish a

ATTORNEY DOCKET NO. 21085.0044U3  
Application No. 10/542,555

*prima facie* case of obviousness, the rejection is improper and will be overturned.” *In re Deuel*, 51 F.3d 1552, 1557, 34 U.S.P.Q.2d 1210 (Fed. Cir. 1995) (citing *Fine*, 837 F.2d at 1074).

Neither Taylor et al. nor Schwiebert et al. teach or suggest that a combination of Zn<sup>2+</sup> and ATP; ivermectin;  $\alpha$ ,  $\beta$ -methylene-ATP; benzoyl-benzoyl-ATP; ATP $\gamma$ S; or AMPPNP, would result in a sustained elevation in cytosolic Ca<sup>2+</sup> levels in the cell. In fact, neither Taylor et al. nor Schwiebert et al. even mention Zn<sup>2+</sup>, much less that there is a sustained elevation in cytosolic Ca<sup>2+</sup> levels in the cell when contacted with this combination. In fact, Schwiebert et al. explicitly states that P2X receptors, upon binding their ATP ligand, may increase cytosolic Ca<sup>2+</sup> levels only transiently. This is in stark contrast to the claims as amended, which discloses that there is a sustained elevation in cytosolic Ca<sup>2+</sup> levels in the cell. Therefore, not only do Taylor et al. and Schwiebert et al. not teach or suggest the claimed invention, they actually teach away from it.

This defect is not corrected by Sperlagh et al., which did not even discuss or measure cytosolic Ca<sup>2+</sup> levels. Although they did measure the outflow of physiological effects in the presence of Zn<sup>2+</sup> and ATP, they found the effect to be transitory in nature (Figure 1, paragraph bridging pages 1777 and 1778). Therefore, one of skill in the art would have believed that cytosolic Ca<sup>2+</sup> would also have been transient in nature. Furthermore, Sperlagh et al. examines guinea pig heart, a very different tissue or cell model preparation than the nose, lung and airways. The effects seen in the guinea pig heart would not necessarily have correlated to the effects seen on epithelial cells.

Applicants therefore respectfully request withdrawal of this rejection.

Favorable consideration of claims 1-3, 12-13, and 21-23 is earnestly solicited.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A Credit Card Payment Form PTO-2038 authorizing payment in the amount of \$510.00, representing a three month extension of time, and a Request for Extension of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge

**ATTORNEY DOCKET NO. 21085.0044U3  
Application No. 10/542,555**

any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.

/Janell T. Cleveland/  
Janell T. Cleveland  
Registration No. 53,848

NEEDLE & ROSENBERG, P.C.  
Customer Number 23859  
(678) 420-9300  
(678) 420-9301 (fax)